

## REMARKS

### **I. Claims in the Case**

Claims 1, 6, 7, 9 and 41 have been amended. Claims 1-7, 9-11, 13, 41, 46 and 47 are pending and under examination.

Claim 1 has been amended to make reference to the promoter being a polymerase III promoter that is regulated by a polypeptide regulator that comprises both a DNA binding domain and a repressor domain. Claim 6 has been amended to clarify that the Tet repressor further includes a repressor domain in addition to its usual DNA binding domain, and also to address the section 112, second paragraph concerns. Claims 7 and 9 have been amended to address the section 112, second paragraph concerns. Claim 41 has been amended to place it into independent form and to introduce the amendments just discussed with reference to claim 1.

### **II. Information Disclosure Statement**

Applicants note the Examiner's comments with respect to references C70 – C303. However, each of these references were submitted to and received by the PTO. See the enclosed copy of the postcard indicating receipt of these references by the PTO. At substantial expense to our client we have enclosed yet another copy of these references.

### **III. Section 112, Second Paragraph Concerns**

Applicants believe that the enumerated section 112, second paragraph, concerns have been addressed by the amendments discussed above.

#### **IV. Anticipation Rejections**

##### **A. *Claims 1-7, 9-11, 13, 41, 46 and 47 over Lois-Caballe et al.***

Applicants have reviewed the Lois-Caballe *et al.* reference and note that the system described there employs a traditional Tet repressor, *i.e.*, a repressor that incorporates only a DNA binding domain and does not appear to include a separate repressor domain (such as might be encoded by a KRAB repressor). Thus, the Tet repressor of Lois-Caballe does not provide the dual safety mechanism of both a DNA binding (*i.e.*, the “steric” hindrance of the traditional Tet repressor) and a separate functional polymerase repressor). Applicants have been unable to identify any teaching or suggestion in Lois-Cabelle to prepare and employ such a dual-functioning repressor.

##### **B. *Claims 1-2, 4-7, 9-11, 13, 41, 46 and 47 over Giordano et al.***

Applicants incorporate by reference the discussion above with respect to Lois-Cabelle *et al.* which is equally applicable to the Giordano *et al.* reference.

##### **C. *Claims 1-2, 10, 13, 41, 46 and 47 over Beach et al.***

Applicants incorporate by reference the discussion above with respect to Lois-Cabelle *et al.* which is equally applicable to the Beach *et al.* reference.

#### **V. Obviousness Rejections**

##### **A. *Claims 1-7, 9-11, 13, 41 and 46-47***

With respect to obviousness, the Action first rejects claims 1-7, 9-11, 13, 41 and 46-47 as obvious over Yao *et al.*, Verma *et al.*, Albashir *et al* EMBO and Albashir *et al.* Nature.

Applicants have reviewed each of these references, and to the extent they disclose the use of a Tet repressor and a Tet operator, they appear to use the traditional scenario employing the naturally occurring Tet repressor, which only incorporates a DNA binding function and thus

serves to repress through its DNA binding activity. The repressor of the present invention has been modified to incorporate a separate RNA polymerase repressor, such as a KRAB, and thus has a dual repressor function that prevents undesirable “leakage.” Applicants have been unable to identify any such teaching or suggestion in the cited references, but would encourage the Examiner to point out any such reference in case Applicants have overlooked it.

Accordingly, it is submitted the claims now define novel and non-obvious subject matter.

***B. Claims 1-7, 9-11, 13, 41 and 46-47***

Lastly, the Action rejects claims 1-7, 9-11, 13, 41 and 46-47 as obvious over the combination of Giordano *et al.*, Elbashir *et al.* EMBO, Elbashir *et al.* Nature, further in view of Verma *et al.*

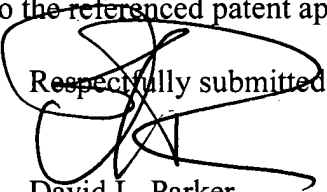
Applicants again respectfully traverse for the reasons stated above and submit that the claims define novel and non-obvious subject matter.

**VI. Reintroduction of Withdrawn Claims**

Assuming that the Examiner agrees that the claims currently under examination define novel and nonobvious subject matter, it is requested that the withdrawn claims that depend from the pending claims be reintroduced for examination on the merits.

**VII. Conclusion**

The Examiner is invited to contact the undersigned attorney at (512) 536-3055 with any questions, comments or suggestions relating to the referenced patent application.

  
Respectfully submitted,

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